OBJECTIVES: The German market access system for drugs have been changed significantly in the last years, by introducing a similar focus on benefit assessment as in the French system. The research question remains whether they produce consistent results in terms of additional benefit (AB) for pharmaceuticals which have passed the assessment in both systems. **METHODS:** The G-BA and IQWiG as well as the Transparency Commission (TC) databases were searched systematically to identify those products, which have been processed in both systems between Jan 2011 and Dec 2013. For further comparison a data grid consisting of 26 items for evaluation has been developed including study comparator, primary clinical endpoints, health related quality of life inclusion. **RESULTS:** Overall, 140 new therapies have been assessed in France by TC, and 80 in Germany by the G-BA. According to inclusion criteria, 44 products could be identified which have passed through both systems including 7 orphan drugs. Thirteen products (30%) had no AB granted by both Agencies, whereas 9 (20%) were in both cases granted with a minor AB, (assuming that "minor" values are equivalent between the two systems), amounting to 22/44 cases with a similar resolution. Five cases (11%) showed a discrepancy in added benefit, all times TC = no and G-BA = yes. However, varying magnitudes appeared to be the greatest difference (n = 17 (39%) remaining drugs), conditioned by lacking concordance of both scale grade systems. **CONCLUSIONS:** Decisions of the agencies in both countries show partial heterogeneity in driving criteria like benefit levels (ASMR and AB). Although the evidence package for initial assessment in both countries is largely similar, preliminary results suggest their contextualization and scales are different. Further analysis based on results of the grid is needed to better assess criteria leading to different benefit levels and their reimbursement impact.

PHP219

FACTORS INFLUENCING DUTCH DRUG REIMBURSEMENT RECOMMENDATIONS; A DATABASE ANALYSIS

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OBJECTIVES: In the Netherlands, manufacturers need to apply for reimbursement of outpatient drugs on either list 1A (no added benefit) or 1B (added benefit). For expensive drugs, hospitals can receive additional reimbursement if the drug is included on the expensive drug list (EDL). Pharmacoeconomic evidence is only required for list 1B and EDL evaluations. The National Health Care Institute (NZi) evaluates submissions and makes (provisional) reimbursement recommendations to the Dutch government. The aim of this study was to identify explanatory variables for the recommendation by NZi. **METHODS:** A database of published evaluations from February-2006 to March-2014 was created, consisting of the final reimbursement recommendation and a range of corresponding explanatory variables such as the therapeutic indication, clinical and economic characteristics. Univariate analyses were performed to assess the impact of the individual explanatory variables on the recommendation by means of odds ratios. **RESULTS:** In total 262 applications were included; the number of positive recommendations by NZi were 121/122 (99%) for 1A, 77/107 (72%) for 1B and 19/28 (68%) for EDL. Pharmacoeconomic analysis was reported in 36/107 (34%) 1B evaluations, of which 27 (75%) were recommended. For the EDL category, pharmacoeconomic analysis was reported in 20/28 (71%) evaluations, out of which 17 (85%) received a positive recommendation. Univariate analyses for the 1B subgroup showed that NZi recommendations were significantly (α=0.05) influenced by clinical trials with life-saving primary endpoint (positive), non-inferior trial outcomes compared to placebo (negative) and budget impact below €2,500,000 (positive). Whereas, the univariate analyses on EDL evaluations demonstrated that ATC-code L (antineoplastic and immunomodulating agents), clinical trials with life-saving primary endpoint and reporting of economic analysis outcomes had a significant and positive impact on the final NZi recommendation. **CONCLUSIONS:** These univariate analyses demonstrated that for 1B and EDL evaluations indication, clinical and economic factors impact the NZi reimbursement recommendations.

PHP220

MEASURING EXTENT OF ACCESS FOR NICE HEALTH TECHNOLOGY ASSESSMENT DECISIONS: TRENDS FROM 2008 TO 2013

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OBJECTIVES: When assessing trends in NICE HTA decisions it would be useful to ascertain their implications on access for groups of technologies. A specific issue is to understand the degree of access associated with 'optimised' decisions, where usage has been restricted to a subgroup of patients relative to the scope of the appraisal. Using a previously developed method, we calculate the degree of recommended access for medicines and assess trends between 2008 and 2013 by therapeutic area and over time. **METHODS:** In a previously published paper we developed a measure, **M**, to assess access associated with NICE technology optimised appraisal decisions. This was defined as **M=(p/P)x100**, where **M** is a measure of the level of patient access (0 equals no access, 100 full access), **P** is the set of patients considered in the guidance as potential candidates for treatment (given the scope of appraisal and license), and p is the number of patients for whom NICE did recommend. Applying measure **M** to NICE HTA decisions for medicines between January 2008 and December 2013 we assess trends by therapeutic area and over time. In this paper, to understand trends, we extend the analysis to include recommended and not recommended decisions. We assume a recommended decision scores 100 using measure **M**, a not recommended decision 0, and optimised decisions, where not possible to determine **M**, a score of 50. **RESULTS:** For 201 decisions between 2008 and 2013, on average, **M** was equal to 52, ranging from 37 in 2008 to 57 in 2011. At therapy level, **M** scored between 38 for cancer medicines to 100 for Hepatitis C treatments. **CONCLUSIONS:** The results for this period suggest around half of patients have been recommended by NICE to receive treatment, relative to scope of appraisal and license. These considerations address access not implementation issues.

PHP221

A COMPARISON OF INTERNATIONAL HEALTH TECHNOLOGY ASSESSMENT SYSTEMS – DOES THE PERFECT SYSTEM EXIST?

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OBJECTIVES: There are a number of common elements considered good practice in Health Technology Assessment (HTA) that have been published by organizations representing the field. These components include: clear processes and decision-making, including scope for pragmatic approaches and appeal; transparency in methodology, value judgments and decisions; and a facility for stakeholder involvement. The objective of this study was to compare international HTA systems to rank their performance against the ideal components of HTA. Information was also collected on emerging topics such as combined regulatory-payer scientific advice, coverage with evidence, evaluation of drug-diagnostic pairs and disinvestment. **METHODS:** A survey was designed to collect information on the HTA systems in the United Kingdom (UK), France, Germany, Italy, The Netherlands, Sweden, Central Eastern Europe, Canada, Australia, New Zealand (NZ), Korea and Taiwan. Questions were grouped under the topics: process, methods, data, societal input and transparency. The survey was completed by Roche affiliates with first-hand experience working with the HTA system in their country. **RESULTS:** The majority of countries give consideration to rare diseases and low budget impact with leniency in decision making and/or process. Transparency in decision-making is lacking in many of the countries surveyed. Whilst consumer members sit on decision-making committees in several countries, only the UK involves a group of citizens in setting the decision making criteria applied by the committee. Combined regulatory-payer scientific advice is only available in European countries. Australia is the only country to evaluate drug-diagnostic pairings for both costs and outcomes. Only the UK and NZ have routine disinvestment reviews. **CONCLUSIONS:** Each country is performing well in some elements of their HTA system, but none met all the requirements of an ideal system. HTA systems can learn from the experiences in other countries when considering improvements to processes and efficiency.

PHP223

TRENDS IN EARLY ENGAGEMENT BETWEEN INDUSTRY AND HTA: ANALYSIS OF SCIENTIFIC ADVICE SERVICE PROVIDED BY NICE SINCE 2009

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OBJECTIVES: Regulatory Scientific Advice (SA) provided by EMA, FDA, MHRA and other agencies is highly demanded by manufacturers but health technology assessment (HTA) scientific advice is still far from becoming a routine step in the product development cycle. NICE has been running an advisory service for 5.5 years. **METHODS:** This work presents analysis of requests to the programme: types of advice projects, number and type of requests per company, clinical indication, stage of clinical development when the advice is sought, reason for seeking advice and current development and regulatory status of products. **RESULTS:** Between 2009 and 2014 NICE conducted 109 advisory projects (107 medicinal products and two diagnostic tests). 23 of these projects were done in parallel with regulatory agencies and/or other HTA bodies. 78% of all requests were in the following four therapeutic areas: oncology, neurology, rheumatology and cardiology. Majority of products (61%) were in phase II of clinical development when advice was sought. At the time of this analysis, 71 products (66%) were still in development, 6 (5.5%) were subject of a review for a marketing authorisation (MA), 8 (7.5%) had received a MA, the authorisation was not granted to 2 products (2%) and the clinical development was discontinued in 20 cases (19%). Most products that received NICE scientific advice are yet to be referred to the technology appraisals programme. **CONCLUSIONS:** Over the last few years, requests for scientific advice diversified into personalised medicines, regenerative medicines and products for rare and very rare diseases. Most HTA scientific advice requests continue to come from top 20 Pharma companies, however we are starting to see an increasing number of inquiries and project bookings from small-medium size companies.

PHP224

EXPLORING UNCERTAINTY IN ECONOMIC EVALUATION OF MEDICINES: A REVIEW OF THE FIRST MANUFACTURERS' SUBMISSIONS TO THE FRENCH NATIONAL AUTHORITY FOR HEALTH (HAS)

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OBJECTIVES: Since October 2013, HAS is required to provide the inter-ministerial Economic Committee on Health Care Products (CEPS) with an economic evaluation on innovative medicines likely to have a significant budget impact on the national health insurance scheme. HAS economic evaluations are based on critical appraisals of cost-effectiveness analyses (CEA) submitted by manufacturers. Exploration of uncertainty around incremental cost-effectiveness ratio is critical to assess the robustness of CEA. Our objective was to assess how uncertainty exploration has been undertaken by manufacturers, using HAS guidelines on economic evaluation as an analytical framework. **METHODS:** Manufacturers' submissions assessed by end of May 2014 (n=13) were reviewed. Three sources of uncertainty were considered: uncertainty around model input parameters, uncertainty around model structure and methodological uncertainty. Tools to explore uncertainty included deterministic sensitivity analysis (DSA), probabilistic sensitivity analysis (PSA), as well as overall compliance with HAS guidelines. **RESULTS:** Model input parameters were the most frequently explored source of uncertainty. Both DSA and PSA were systematically used. However, reporting of DSA varied substantially across submissions, with frequent lack of justification of parameters ranges. Regarding PSA, the choice of distribution was not systematically justified and lacked consistency across similar parameters. Most submissions failed to consider parameters correlations. Exploration of uncertainty around model structure was rarely presented. Where applicable, alternative methods for extrapo-

lating health outcomes were reported in two-thirds of the submissions. However, worst-case scenarios were hardly presented. Compliance with HAS guidelines for exploring methodological uncertainty (e.g. perspective, discounting, time horizon) was fair. However, the choice of the comparator(s)–an essential component of a CEA–was considered problematic in nearly 40% of submissions. **CONCLUSIONS:** Overall, reporting of DSA and PSA is complying with HAS guidelines. More work is needed to explore uncertainty, in particular, to account for correlations between model input parameters and to enhance the analysis of structural uncertainty.

PHP225

CONDITIONAL RESOLUTIONS IN THE AMNOG EARLY BENEFIT ASSESSMENT

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OBJECTIVES: Since 2011 the early benefit assessment (EBA) is mandatory to obtain reimbursement for new drugs in Germany. By law EBA of the G-BA (Federal Joint Committee) can be conditional for a certain period of time. This study explores the number, duration and rationale of conditional G-BA resolutions. Furthermore the provided, later given (during statement process), accepted and additionally requested study data is analysed in this context. **METHODS:** AMNOG dossiers and resolutions of the G-BA including justifications until June 2014 were reviewed for relevant information and analysed with special regard to the submitted and accepted study data. Drugs which were directly allocated to a fixed-reference price group were excluded. **RESULTS:** 22 new drugs with conditional resolutions were identified (29.3% of all resolutions; 2012: 6, 2013: 10, 2014: 6). Duration varied between 1 and 5 years (1: 4, 2: 8, 3: 5, 4: 1, 5: 4). Conditional resolutions were most common in cancer (n=13; 59.1%) drugs. 91.0% had at least a benefit (none: 2, minor: 12, considerable: 6, not quantifiable: 2) in one subgroup. G-BA limited resolutions due to (a) no sufficient data to assess the benefit (n=9), (b) conditional approval and/or further data requests by EMA (European Medicines Agency) (n=6), (c) expected new study results (n=6), and (d) due to a formal incorrect dossier (n=1). To date, only vemurafenib was assessed again with same result as before. **CONCLUSIONS:** From 2011 on an increased number of resolutions and especially cancer drugs were conditional. Only in a few cases G-BA defined in the resolution which specific data has to be shown in the re-assessment. In these cases the requirements concerning further evidence were not part of the G-BA voting. As currently just one drug was re-assessed, no conclusions can be drawn how re-assessment changes the extent or certainty of additional benefit.

PHP226

PRICING ADDITIONAL BENEFIT IN GERMANY

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OBJECTIVES: Gemeinsame Bundesausschuss (G-BA) assesses the additional benefit of newly-approved drugs compared to the G-BA-determined appropriate comparator. As part of the submission, manufacturers provide annual drug cost estimates. This research tests whether manufacturers submit higher annual costs for drugs that provide greater additional benefit, that is, whether added benefit is priced. **METHODS:** The influence of G-BA's additional benefit assessment on the manufacturer's estimated per patient annual drug cost was estimated via ordinary least squares based on 73 reviews. The model also included controls for the (log) size of the target population and the annual cost of the comparator. These variables were collected from the Federal Gazette publication or the "Beschluss" document. **RESULTS:** Our model explains three-quarters of the variation in annual drug cost (R^2=.76). Conditional on the target population and the cost of its comparator, a drug assessed as having unquantifiable or minor added benefit is estimated to have a per patient annual cost about 2 times greater than one with no added benefit (p=.02). A drug with the highest assessment, "Considerable additional benefit," is estimated to have an annual per patient cost that is 9 times greater (p<.01). There is evidence of a "quantity discount": doubling the size of the target population is estimated to reduce the per-patient annual cost by 18% (p<.01). **CONCLUSIONS:** If, as seems plausible, manufacturers' assessments of their own drugs are aligned with G-BA's assessments, our results are consistent with manufacturers setting higher prices for more beneficial drugs. The price a manufacturer uses to estimate annual cost represents in effect a proposed allocation of its drug's benefits between itself and patients/payers. This research raises at least two important questions: How do manufacturers propose to share the gains and what sharing emerges from subsequent price negotiations?

PHP227

RISK OF BIAS IN TRIAL-BASED ECONOMIC EVALUATIONS

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OBJECTIVES: The objective of our research is to give first an overview of the risks of bias in trial-based economic evaluation, and second to identify how key sources for bias can be revealed and overcome (bias-reducing strategies) in future trial-based economic evaluation in the fields of general practice and health psychology. **METHODS:** A scoping review was performed using PubMed and the NHS Economic Evaluation data base. It was complemented with experiences of the authors. Sources of bias in trial-based economic evaluation as well as bias-reducing strategies are discussed. **RESULTS:** The different forms of bias are presented, and assigned to a particular trial phase. A distinction is made between pre-trial biases, biases during the trial and biases that are relevant after the actual trial. All potential forms of bias are discussed in detail and strategies are shown to detect and overcome these biases. **CONCLUSIONS:** In order to avoid bias in trial-based economic evaluations, one has to be aware of all of the possible forms of bias and all stakeholders have to examine trial-based economic evaluations in a rigorous and stringent manner. Our research findings can be helpful in this examination as they provide an overview of the possible biases which researchers should take into account.

PHP228

UK VALUE-BASED ASSESSMENT: WILL SCOTLAND'S SMC APPROACH IT IN THE SAME WAY?

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OBJECTIVES: In May 2010 the UK government set out its intentions to reform the current method of pricing branded medicines and introduced a new system of value-based pricing (VBP). This was to replace the Pharmaceutical Price Regulation Scheme (PPRS) which expired at the end of 2013. With discussion still ongoing, and the PPRS renewed up until end of 2018, it has been indicated that VBP will no longer relate to medicines' pricing, but instead will be a reshaping of the Health Technology Assessment (HTA) model employed by the UK in its appraisal of new medicines, and renamed Value Based Assessment (VBA). As medicine assessment is devolved in the UK, performed by NICE in England and the SMC in Scotland, we seek to understand whether the SMC will adopt the same approach to VBA as NICE. **METHODS:** The research was conducted through in-depth secondary research and interviews with stakeholders, including payers and KOLs, in UK. **RESULTS:** Both NICE and the SMC have indicated they will continue to use QALY as a measurement of clinical and cost effectiveness while also incorporating issues such as burden of illness and wider societal impact in their assessment. However, their approach to conducting such assessments may differ with the SMC suggesting using a new system of patient and clinician engagement (PACE), currently in use for the appraisal of medicines for end of life or rare conditions (orphans), as a wider process to determine Scotland's requirement for a value based approach to assess all new medicines. **CONCLUSIONS:** Manufacturers would be encouraged to closely follow the outcomes from the new PACE system, incorporated into the SMC assessment for end of life and orphan therapies, to ensure readiness for the introduction of VBA in Scotland.

PHP229

DISCREPANCY BETWEEN NATIONAL DRUG RECOMMENDATIONS AND LOCAL UPTAKE IN THE SWEDISH INPATIENT SECTOR

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OBJECTIVES: The current study seeks to assess discrepancies between national inpatient drug recommendations issued through the cost-effectiveness pilot project (Klinikläkemedelsprojektet) in Sweden and local uptake reflected by Stockholm Country Council´s (SLL) procurement activity. **METHODS:** Secondary research investigated the 15 inpatient drug recommendations issued by the national New Pharmaceutical Therapies group (Nya Lakemedels Terapier, NLT) in 2013 and compared these against the SLL's 2014 procurement list. **RESULTS:** In 2013, the NLT group issued a total of 15 recommendations for products in a variety of therapeutic areas (TA). Out of these, ten gained positive national decisions, 50% of which were for oncology drugs. Of those recommended, cancer drug pertuzumab (Perjeta; Roche, Switzerland) saw the highest incremental cost-effectiveness ratio (ICER), at SEK2,565,000 (USD383,730) per quality-adjusted life year (QALY) - greatly exceeding the informal cost-effectiveness threshold of SEK800,000 in Sweden. There was a significant discrepancy in the number of nationally recommended drugs (ten) in 2013, versus the SLL uptake (two) by 2014. The two recommended products subsequently procured were Roche´s (Switzerland) ophthalmology drug ranibizumab (Lucentis) and Takeda´s (Japan) oncology therapy brentuximab vedotin (Adcetris). **CONCLUSIONS:** The Swedish government is contemplating making the Klinikläkemedelsprojektet permanent, and as such the alignment between national and local level priorities is a critical component of its integrity. The results show that eight nationally recommended products had not been procured, indicating that there is still a discrepancy between those recommendations and uptake at the local level, based on the current data. One explanation for the discrepancy could be attributed to the funding system, where local payers are responsible for funding inpatient drugs.

PHP230

HTA APPROACH IN ITALY. STRUCTURE, METHODS, AND PROCESS OF VENETO REGION'S EVALUATION OF PHARMACEUTICAL EFFECTIVENESS UNIT (UNITÀ DI VALUTAZIONE DELL'EFFICACIA DEL FARMACO, UVEF)

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OBJECTIVES: Veneto leads the nation in terms of better health status and pharmaceutical expenditures within budget. This study aimed to assess the region's Health Technology Assessment (HTA) approach (structure, methods, and process of conducting HTA) by observing Evaluation of Pharmaceutical Effectiveness Unit's (UVEF) evaluations on drugs, the concomitant Regional Technical Commission (CTR) decisions on formulary inclusion, and the evidences considered. **METHODS:** We reviewed all HTA reports in the UVEF website evaluating the HTA dimensions assessed, if they were in line with the HTA scoping document by the Regional Decrees (2008), and changes over time. Further, this research evaluated the presence of explicit explanations behind each CTR decision. **RESULTS:** 223 HTA listings were retrieved in the UVEF website (2004-2011). 50.23% were published before the actual establishment of UVEF (2008) and were probably labelled HTA retrospectively. Fewer dimensions were assessed in the earlier documents and the most extensive changes were seen in 2008. The most assessed dimensions were Efficacy, Safety, and Costs and the least assessed were Budget Impact Analysis, Target Population, Place in therapy, and Assessment of Innovation. The Regional Decrees (2008) were impactful on the structure of the HTA reports, however these are still not fully compliant to the scoping document. A total of 72 CTR decisions were found in the website from 2009 to 2011. On average, 92% of all CTR documents have a documented explanation behind each decision. **CONCLUSIONS:** The HTA approach in Veneto is evolving towards the development of uniformity in the documents and a single transparent approach. The upward trend of attaching CTR decisions with explicit explanations